

PCT

WORLD INTELLECTUAL PROPERTY
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER

WO 9606826A1

(51) International Patent Classification ⁶ : C07C 311/65		A1	(11) International Publication Number: WO 96/06826
			(43) International Publication Date: 7 March 1996 (07.03.96)
(21) International Application Number: PCT/US95/08966 (22) International Filing Date: 21 July 1995 (21.07.95) (30) Priority Data: 08/297,465 29 August 1994 (29.08.94) US (60) Parent Application or Grant (63) Related by Continuation US 08/297,465 (CIP) Filed on 29 August 1994 (29.08.94) (71) Applicant (for all designated States except US): E.I. DU PONT DE NEMOURS AND COMPANY [US/US]; 1007 Market Street, Wilmington, DE 19898 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): ADJEI, David, Akuteh [US/US]; 3 Pierson Drive, Hockessin, DE 19707-1005 (US). BLAISDELL, Charles, T. [US/US]; 855 Shallcross Lake Road, Middletown, DE 19709-8937 (US). (74) Agents: KATZ, Elliott, A. et al.; E.I. du Pont de Nemours and Company, Legal Patent Records Center, 1007 Market Street, Wilmington, DE 19898 (US).		(81) Designated States: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG). Published With international search report.	
(54) Title: IMPROVED PROCESS FOR MAKING SULFONYL ISOCYANATES			
(57) Abstract			
This invention relates to an improved method of making sulfonyl isocyanates from the corresponding sulfonamides and phosgene.			

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

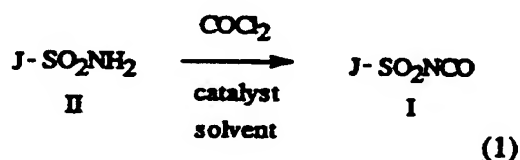
TITLE**IMPROVED PROCESS FOR MAKING SULFONYL ISOCYANATES****BACKGROUND OF THE INVENTION**

The present invention pertains to an improved process for making sulfonyl isocyanates from the corresponding sulfonamides and phosgene. Sulfonyl isocyanates are useful intermediates in the preparation of fine chemicals such as pesticides, including sulfonylurea herbicides, and pharmaceuticals.

U.S. 4,238,621 discloses the preparation of sulfonyl isocyanates from a reaction mixture of the corresponding sulfonamides and phosgene wherein the sulfonamide is generally present in molar excess in the reaction mixture relative to phosgene. In the present invention, the phosgene is always in molar excess relative to sulfonamide, thereby providing better yield and shorter reaction times.

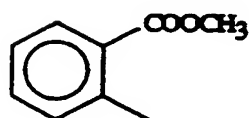
SUMMARY OF THE INVENTION

The present invention pertains to an improved process for the preparation of sulfonyl isocyanates of Formula I comprising adding the corresponding sulfonamide of Formula II in small increments or continuously, preferably continuously, to a reaction mixture comprising inert solvent, phosgene and catalyst according to equation 1

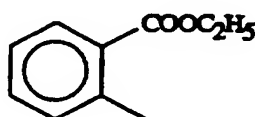


wherein

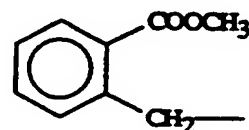
J is



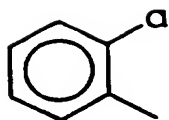
J-1



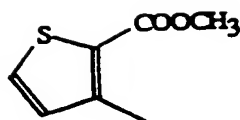
J-2



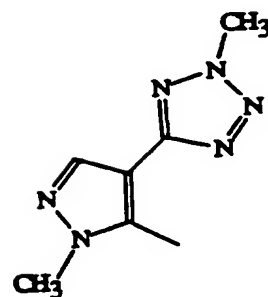
J-3



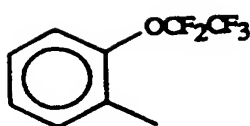
I-4



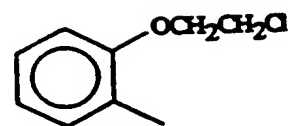
I-5



I-6



I-7



I-8

- 5 such that there is in the reaction mixture an excess of phosgene relative to sulfonamide.
The most preferred sulfonyl isocyanate is methyl 2-(isocyanatosulfonyl)benzoate.

DETAILED DESCRIPTION OF THE INVENTION

According to the present invention, sulfonamide II is fed to a reaction mixture of inert solvent, catalyst and phosgene wherein it is converted to isocyanate I. Elevated
10 temperatures, typically in the range of 100° to 200°C, preferably 120° to 135°C, are usually required to make the reaction proceed at practical rates. Pressure can be ambient up to about 2 atmospheres (about 200 kPa). Phosgene is replenished to the reaction mixture so that at any point during the reaction there is always present a molar excess of phosgene (hereinafter referred to as "phosgene-rich") relative to sulfonamide; preferably
15 there is at least 2% by weight of phosgene in the reaction mixture, more preferably at least 5%. Sulfonamide can be fed to the reaction mixture in small increments or continuously, preferably continuously, and can be in the form of a slurry or solution in solvent, preferably as concentrated as possible. The slurry can be preheated before admission to the reactor.

20 Solvent can be any inert solvent with a boiling point at or above the desired reaction temperature; examples include xylene, chlorobenzene, mesitylene, toluene, pentachloroethane and octane.

Catalysts include (U.S. 4,238,621) carbaryl isocyanates such as butyl isocyanate and tertiary amines such as 1,4-diaza[2,2,2]bicyclooctane (DABCO). The full charge of
25 catalyst can be added to the initial reaction mixture, or added incrementally or continuously during the course of reaction. Feeding the catalyst over the course of the reaction can reduce the total amount of catalyst needed and reduce side reactions.

Catalysts also include sulfonyl isocyanates (Res. Discl. (1983) 23210, 261), preferably the product sulfonyl isocyanate. The sulfonyl isocyanate need not be isolated, and a small portion of the product reaction mixture (referred to as a "heel") from a previous batch can be employed as catalyst in a subsequent batch.

5 The reaction of sulfonamide and phosgene is very rapid and exothermic, and HCl is generated as a byproduct. It is preferable to drive the HCl out of the reaction mixture as rapidly as possible, preferably by maintaining vigorous reflux of phosgene, so that side-reactions caused by the HCl, and the resulting yield losses, are minimized. The HCl off-gas will typically be captured by scrubbers so as to avoid release to the environment; the
10 phosgene can be condensed and returned to the reaction mixture. The HCl generation can be used to monitor the course of the reaction and can also be used to maintain an appropriate sulfonamide feed rate and concentration so that the reaction is kept under control and reaction times are as short as possible.

15 Once the reaction is complete, excess phosgene and dissolved HCl can be removed from the mixture by standard methods such as distillation. The sulfonyl isocyanate can be recovered by standard methods, such as crystallization and filtration. Alternatively, the sulfonyl isocyanate can be reacted further, with or without isolation, to form, for example, a sulfonylurea herbicide as described in U.S. 4,238,621, column 5, lines 14-20.

20 In accordance with this invention, improved yields of sulfonyl isocyanate are obtained with less reaction time. The critical feature of the present invention is the reaction of sulfonamide in a phosgene-rich environment throughout substantially the entire process. In contrast, known methods for producing sulfonyl isocyanate from sulfonamide add phosgene to a reaction mixture of sulfonamide such that throughout substantially the entire reaction the sulfonamide is in excess relative to phosgene.

25 EXAMPLES

 The examples which follow demonstrate the improved process of the present invention. Comparative Example A is provided as an illustration of the state of the art as disclosed in U.S. 4,238,621 and Res. Discl. (1983) 23210, 261. The same reactor was employed throughout. In all examples the sulfonyl isocyanate is methyl
30 2-(isocyanatosulfonyl)benzoate and the sulfonamide is methyl 2-(aminosulfonyl)-benzoate.

 The reactor is a Pfaudler 7500 L reactor which was jacketed for steam heating and which was equipped with a reflux condenser capable of cooling to -30°C to recover refluxing phosgene. The reactor has an inlet port for admitting reactants, an exit port for
35 recovering product and an agitator for thorough mixing of ingredients during reaction.

Summary of Ingredients and Parameters

	Example 1	Example 2	Example 3	Example A
Sulfonamide (kG)	771.8	1452.8	1589	771.8
Butyl isocyanate (kG)	32	72.6	72.6	71.7
Xylene (kG)	2679	2679	2679	2679
*Heel (kG)	898.9	911.6	961.6	972.5
Reaction Temperature (°C)	126-130	126-130	126-130	126-130
Reaction time (hours)	2.5	7.2	7.5	3.4
% yield sulfonyl isocyanate (based on sulfonamide)	95.1	94.4	95.1	87.7

*Heel is comprised of sulfonyl isocyanate and solvent, and is the product reaction mixture from a previous batch.

Example 1

A heel from a previous batch was present in the reactor. A slurry of xylene and sulfonamide was made in a separate vessel. The reactor was heated to about 130°C after which phosgene was added until the reactor mixture was saturated with same (about 3 % by weight of the reaction mass) at 127°C. While maintaining vigorous reflux conditions, continuous feed of sulfonamide slurry and butyl isocyanate was started simultaneously. The slurry feed rate was 2 kG/min; the butyl isocyanate rate was about a 10% molar ratio relative to sulfonamide and was maintained throughout the entire course of slurry addition. The operating pressure was monitored as an indication of HCl off-gas generation. During the course of the reaction, phosgene was replenished to the reactor as needed to maintain reaction temperature and so that the reaction mixture was always saturated with same. When the reaction was complete, the residual HCl and phosgene was stripped from the reaction mixture by solvent distillation and by sparging with nitrogen under reflux and as the reaction mixture cooled. The reaction mixture was analyzed for sulfonyl isocyanate and the yield calculated.

Example 2

Example 2 was run as described in Example 1 except using the quantities and conditions noted in the summary above.

Example 3

Example 3 was run as described in Example 1 except using the quantities and conditions noted in the summary above.

Comparative Example A

A heel from a previous batch was present in the reactor. The sulfonamide was slurried with xylene in a separate vessel and then the entire charge was transferred to the reactor containing the heel. The butyl isocyanate was then added to the reactor after which the reactor was brought up to reaction temperature. The continuous phosgene feed was then started at a rate of about 150 kG/hr, and adjusted as necessary to maintain

a steady operating operating pressure as HCl is generated. When the reaction was complete, as indicated by the cessation of phosgene consumption, the residual HCl and phosgene was stripped from the reaction mixture by solvent distillation and by sparging with nitrogen under reflux and as the reaction mixture cooled. The reaction mixture was
5 analyzed for sulfonyl isocyanate and the yield calculated.

CLAIMS

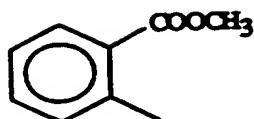
1. In a process for making a compound of the formula



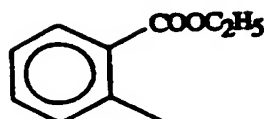
5

wherein

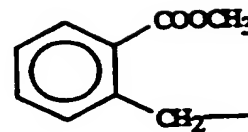
J is



J-1

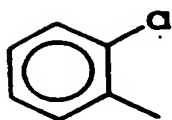


J-2

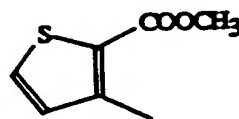


J-3

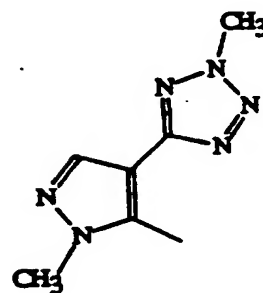
10



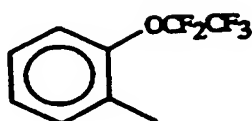
J-4



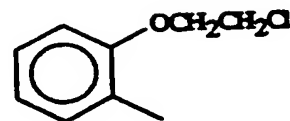
J-5



J-6



J-7



J-8

- 15 by reacting a compound of the formula $J-SO_2NH_2$ with phosgene in a reaction mixture comprising the compound $J-SO_2NH_2$, phosgene and a solvent, the improvement comprising conducting the reaction in the presence of a molar excess of phosgene relative to the compound $J-SO_2NH_2$.

2. The process of Claim 1 wherein the percent by weight of phosgene in the
20 reaction mixture is at least 2%.

3. The process of Claim 2 wherein the percent by weight of phosgene in the reaction mixture is at least 5%.

4. The process of Claim 1 wherein J is J-1.

INTERNATIONAL SEARCH REPORT

Intern: Application No

PCT/US 95/08966

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07C311/65

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP,A,0 034 431 (DU PONT) 26 August 1981 see claims; examples 1,2 ---	1-4
A	US,A,3 371 114 (SAYIGH ET. AL.) 27 February 1968 see whole document ---	1-4
A	EP,A,0 046 626 (DU PONT) 3 March 1982 cited in the application see claims; examples -----	1-4

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

3 November 1995

Date of mailing of the international search report

21.11.95

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+ 31-70) 340-3016

Authorized officer

Helps, I

[Handwritten signature]

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 95/08966

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
EP-A-0034431	26-08-81	US-A-	4305884	15-12-81
		AU-B-	6684881	13-08-81
		JP-A-	56125356	01-10-81
		US-A-	4892946	09-01-90

US-A-3371114	27-02-68	NONE		

EP-A-0046626	03-03-82	AR-A-	221094	30-12-80
		AT-B-	371668	25-07-83
		AU-B-	530575	21-07-83
		CA-A-	1129857	17-08-82
		CA-C-	1199033	07-01-86
		EP-A, B	0007687	06-02-80
		JP-A-	55013266	30-01-80
		SU-A-	1836014	23-08-93
		US-A-	4394506	19-07-83
		US-A-	4383113	10-05-83
		US-A-	4238621	09-12-80
		US-A-	4687507	18-08-87
		AU-B-	4754579	03-01-80
		US-A-	4536576	20-08-85
		US-A-	4564384	14-01-86
		US-A-	4591378	27-05-86
		US-A-	4818278	04-04-89
		US-A-	4721520	26-01-88
		US-A-	4755216	05-07-88
		US-A-	4647303	03-03-87